

EXHIBIT A

JC068 U.S. PRO
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#!/internet/bin/perl5.002 -w

# Copyright (c) 1998
#           Eugene Wang

# *** BEGIN ***
#
#-----#
#input sequence (File 0) to compare
#-----#
if ($#ARGV < 2) {die "argv < 2";}
open(EnzymeInput,$ARGV[0]) || die "Cannot open input file $ARGV[0]";

#print "Input Enzyme 1 sequence = ";
$E1sequence = <EnzymeInput>;
chomp $E1sequence;
$lenE1Seq = length($E1sequence);
$E1sequence =~ tr/a-z/A-Z/;

$E1ExtLoc = <EnzymeInput>;
chomp($E1ExtLoc);
$lenE1Total = $lenE1Seq + $E1ExtLoc;

#print "Input Enzyme 2 sequence = ";
$E2sequence = <EnzymeInput>;
chomp $E2sequence;
$E2sequence = reverse($E2sequence);
$lenE2Seq = length($E2sequence);
$E2sequence =~ tr/a-z/A-Z/;

$E2ExtLoc = <EnzymeInput>;
chomp($E2ExtLoc);
$lenE2Total = $lenE2Seq + $E2ExtLoc;

$lenE1Extra = $E2ExtLoc - $E1ExtLoc;

$E1SizeStart = <EnzymeInput>;
chomp($E1SizeStart);
$E1SizeEnd = <EnzymeInput>;
chomp($E1SizeEnd);

#-----#
#open input FASTA file (File 1)
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#-----
#-----#
#print "Input file name = ";
#$fname = <>;
#chomp $fname;
#$fname = "H_DJ0167F23.seq";
#-----#
open(Infle,$ARGV[1]) || die "Cannot open input file $ARGV[1]";
#-----#
#open output file (File 2)
#-----#
open (Outfile,>$ARGV[2]) || die "Cannot open output file $ARGV[2]";
#open (Outfile,>"output.txt");
#print Outfile "Qualifier\tSequence";
#-----#
#read input FASTA file
#-----#
$line = <Infle>;      #header line
print Outfile "$line";
$linecount = 0;
$FullSeq = "";
#-----#
#check headerline format
#-----#
chomp $line;
@fields = split (/|\|/, $line);

$ntokens = 0;
foreach (@fields) {$ntokens++}
#$ntokens = @fields;

if ($ntokens > 3)
    {$FragmentID = $fields[3];}
else
{
    $line =~ s/^> />/;
    @fields = split (/ /, $line);
    $ntokens = 0;
    foreach (@fields) {$ntokens++}
    if ($ntokens > 0)
        {$FragmentID = $fields[0]; $FragmentID =~ s/^>//;}
    else
        {$FragmentID = "UnknownFragment";}
}

while ($line = <Infle>)      #read in a line
{

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print Outfile "Enzyme top strand: ";
print Outfile "(5\'-$E1sequence";
if ($E1ExtLoc>0) {print Outfile "(N)$E1ExtLoc";}
print Outfile "-3')";
print Outfile "\n";

print Outfile "Enzyme bottom strand: ";
print Outfile "(5\'-";
if ($E2ExtLoc>0) {print Outfile "(N)$E2ExtLoc";}
print Outfile "$E2sequence-3')";
print Outfile " or ";
my $ts = reverse($E2sequence);
print Outfile "(3\'-$ts";
if ($E2ExtLoc>0) {print Outfile "(N)$E2ExtLoc";}
print Outfile "-5')";

print Outfile "\n";

print Outfile "Segment size: $E1SizeStart - $E1SizeEnd\n";

$minLen = $lenE1Total < $lenE2Total ? $lenE1Total : $lenE2Total;
$maxLen = $lenE1Total > $lenE2Total ? $lenE1Total : $lenE2Total;

$NMatchE1 = 0;
$NSelected = 0;
@EnzLocLeft = ();
@EnzLocRight = ();
@EnzTypeLeft = ();
@EnzTypeRight = ();

if ($minLen > 0)
{
    for ($i=0; $i <= $lenFullSeq-$lenE1Seq; $i++)
    for ($i=0; $i <= $lenFullSeq-$maxLen; $i++)
    {
        if (substr($FullSeq,$i,$lenE1Seq) eq $E1sequence)
        {
            $EnzLocLeft[$NMatchE1] = $i + $lenE1Total;
            $EnzTypeLeft[$NMatchE1] = 1;
            push(@EnzLocLeft,$i + $lenE1Total);
            push(@EnzTypeLeft,1);

            print Outfile "$NMatchE1\t$i\t";
            print Outfile "type 1\t";
            print Outfile "$E1sequence\t";
            print Outfile substr($FullSeq,$i,$lenE1Total);
            print Outfile "\n";

            if ($NMatchE1 > 0)
            {
                push(@EnzLocRight,$i + $lenE1Total-1);
                push(@EnzTypeRight,1);
            }
        }
    }
}

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                $nMatchE1++;
            }
        if (substr($FullSeq,$i+$E2ExtLoc,$lenE2Seq) eq
$E2sequence)
        elsif (substr($FullSeq,$i+$E2ExtLoc,$lenE2Seq) eq
$E2sequence)
        {
#           $EnzLocLeft[$nMatchE1] = $i;
#           $EnzCutLeft[$nMatchE1] = 2;
#           push(@EnzLocLeft,$i);
#           push(@EnzTypeLeft,2);

#           print Outfile "$nMatchE1\t$i\t";
#           print Outfile "type 2\t";
#           print Outfile "$E2sequence\t";
#           print Outfile substr($FullSeq,$i,$lenE2Total);
#           print Outfile "\n";

#           if ($nMatchE1 > 0)
#           {
#               push(@EnzLocRight,$i-1);
#               push(@EnzTypeRight,2);
#           }

                $nMatchE1++;
        }
    }

    if ($nMatchE1 > 0)
    {
        push(@EnzLocRight,$i-1);
        push(@EnzTypeRight,2);
    }

    print Outfile "Number of segments: $nMatchE1\n";
    if ($nMatchE1 != ($#EnzLocRight+1)) {die ("Counting
error...$nMatchE1($nMatchE1) != $#EnzLocRight");}
    print Outfile "Matched loci:\n";

    for ($i=0; $i < $nMatchE1; $i++)
    {
        print Outfile "$EnzLocLeft[$i]\t";
    }

    print Outfile "\nSegment Size:\n";
    for ($i=0; $i < $nMatchE1-1; $i++)
    {
        $tmpSegSize = $EnzLocRight[$i] - $EnzLocLeft[$i] + 1;
        if ($tmpSegSize >= $E1SizeStart && $tmpSegSize <=
$E1SizeEnd)
        {
            $SegSelected[$nSelected++] = $i;
        }
    }
}

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        }
        print Outfile "$tmpSegSize\t";
    }
}

#-----
#-----#
##      print out the Segment (E1) sequences
#-----#
print Outfile "\nSegments Selected ($nSelected):";
for ($i=0; $i < $nSelected; $i++)
{
    $selSeq = $SegSelected[$i];
    $Elleft = $EnzLocLeft[$selSeq];
    $Elright = $EnzLocRight[$selSeq];

    if ($lenElExtra > 0) {$Elright += $lenElExtra;}
    else {$Elleft += $lenElExtra;}
    $lenSelSeq = $Elright - $Elleft + 1;

    $OutputHeaderLine = ">" . $FragmentID . "_" . $selSeq . "\tsize=" .
$lenSelSeq;
    $OutputHeaderLine .= "\tLoci=" . $Elleft . "-" . $Elright;
    $OutputHeaderLine .= "\tEnz$EnzTypeLeft[$selSeq]-"
Enz$EnzTypeRight[$selSeq]";

    print Outfile "\n$OutputHeaderLine";
    print "$OutputHeaderLine";

#      Segment sequence
$SeqEltoNextEl = substr($FullSeq,$Elleft,$lenSelSeq);
print Outfile "\n$SeqEltoNextEl\n";
print "\n$SeqEltoNextEl\n";

}

return ($lenFullSeq);
}

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EXHIBIT B

```

#!/internet/bin/perl5.002 -w

*****
# Copyright (c) 1998
# Author: Eugene Wang
# Title: Ligate
# Purpose: Find matching segments/sequences in two files
*****
if ($#ARGV != 2) {die "Number of argv ($#ARGV+1) != 3";}

#-----
#-----#
#input file
#-----#
open(InfleLigate,$ARGV[0]) or die "Open error...$ARGV[0]\n";

$locLigate = <InfleLigate>;
chomp $locLigate;
$seqLigate = <InfleLigate>;
chomp $seqLigate;

close (InfleLigate);
#-----
#-----#
#output file
#-----#
open(Infle,$ARGV[1]) or die "Open error...$ARGV[1]\n";

$OutName = $ARGV[2];
open (Outfile,>$OutName) or die("Open error...$OutName");

$alreadyReadOne = 0;
$sequence = "";
while ($line = <Infle>)      #read in a line
{
    chomp $line;
    next if ($line eq "");
    if ($line =~ /^#/ || $line =~ /^>/)      ##if first char is a '#'
or '>' {
        if ($alreadyReadOne == 1) {
            if (&Ligate($sequence,$locLigate,$seqLigate) == 1) {
                print Outfile "$headerLine\n";
                print Outfile "$sequence\n";
            };
            $sequence = "";
        }
    }
}

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$headerLine = $line;
$alreadyReadOne = 1;
}
else
{
    $sequence .= $line;
}
}

if ($alreadyReadOne == 1) {
    if (&Ligate($sequence,$locLigate,$seqLigate) == 1) {
        print Outfile "$headerLine\n";
        print Outfile "$sequence\n";
    };
}
close (Infile);
close (Outfile);

#####
##### #compare sequence with Ligation Adapter sequence #####
#####
sub Ligate()
{
local $retcode = 0;

local ($seq,$locLigate,$seqLigate) = @_;
local $lenLigate = length($seqLigate);
local $lenSeq = length($seq);

if ((substr($seq,$locLigate,$lenLigate) eq $seqLigate) &&
    (substr($seq,$lenSeq-$locLigate-$lenLigate,$lenLigate) eq
$seqLigate)) {
    $retcode = 1;
}

return $retcode;
}

```